REMARKS

Applicant, through the undersigned, wishes to thank Examiner Kaushal for the courtesy extended on behalf of the applicant during a telephone interview conducted with the undersigned on November 1, 2001.

In the Final Action dated February 12, 2001, claims 1-4 and 6-45 are pending. Claims 6-33 are withdrawn from consideration as drawn to non-elected inventions. Claims 1-4 and 34-45 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification.

This response addresses the Examiner's rejection and the amendment to the claims is consistent with the Examiner's recommendations during the telephone interview. Applicant therefore respectfully submits that the present application is in condition for allowance or at least better condition for appeal. Favorable consideration of all pending claims is therefore respectfully requested.

By way of the foregoing amendment, claims 6-33 have been canceled without prejudice. Applicant reserves the right to file one or more divisional applications directed to the subject matter of these claims.

Turning to the rejection of claims 1-4 and 34-45 under 35 U.S.C. §112, first paragraph, the Examiner contends that the invention as claimed encompasses any and all synthetic genes or derivatives of target genes. The Examiner alleges that the specification does not adequately teach what additional sequences may be added, deleted and/or substituted in the target gene to obtain the instantly claimed synthetic gene. According to the Examiner, as the art does not provide an accepted definition of the term "gene", elaboration of a synthetic gene would require both a disclosure of a definition and characterization of the synthetic gene sequence. The

Examiner indicates that the invention as claimed reads on a combination of multiple gene sequences, wherein the role of each component has not been ascribed. Thus, the Examiner is of the opinion that it is unclear as to how one skilled in the art would use the invention as claimed to modify an unknown target gene in a cell, tissue, organ in an animal. Furthermore, the Examiner contends that the instant claims relate to the art of gene therapy, which was regarded at the time of the instant filing as highly unpredictable. The Examiner argues that the specification does not describe a single working example that demonstrates the delivery or expression of any synthetic gene in an animal. Thus, the Examiner concludes that one skilled in the art would not be able to practice the claimed invention without undue experimentation.

Applicant respectfully disagrees with the Examiner. It is respectfully submitted that the instant specification adequately teaches one skilled in the art how to make and use the claimed invention. In the first instance, the specification provides definitions for the terms "gene" (page 6, lines 17-29), "synthetic gene" (page 7, lines 1-3), "structural gene" (page 7, lines 5-14) and "target gene" (page 7, lines 17-20), all of which are consistent with the definitions of these terms recognized by those skilled in the art. In addition, the specification teaches the essential characteristics of the claimed synthetic genes and genetic constructs; e.g., the synthetic genes and genetic constructs comprise promoter(s), transcription terminator(s) and at least one structural gene sequence(s) required for downregulation of an endogenous target gene. Applicant further submits that a principal feature of the claimed synthetic genes and genetic constructs is a combination of multiple structural gene sequences, each of which comprises a nucleotide sequence substantially identical to a target gene in a cell. In addition, the specification exemplifies a number of genetic constructs as claimed by way of the drawings (for example, Figures 13-15, 19-20 and 22).

However, Applicant has amended the claims in an effort to favorably advance the prosecution of the present case. Specifically, claims 1-4, 34-35 and 39-45 have been canceled without prejudice. Claims 36-38 have been amended and claims 46-47 have been added. Claims 36-37 as amended are drawn to a genetic construct comprising multiple structural gene sequences placed operably under the control of a single promoter, wherein each of said structural gene sequences is identical to a target gene in a cell, and at least one structural gene sequence is placed in the sense orientation under the control of the promoter, and at least one other structural gene sequence is placed in the antisense orientation under the control of the promoter. Claim 46 is also drawn to a genetic construct, which comprises two structural gene sequences, one placed in the sense orientation, the other in the anti-sense orientation relative to the promoter. Claim 38 as amended is drawn to a cell comprising the genetic construct of any one of claims 36-37 or 46. Claim 47 further delineates the genetic construct of any one of claims 36-37 or 46 as comprising at least one of an origin of replication or a selectable marker gene.

It is respectfully submitted that in light of the teachings provided in the present specification and the established prior art methodologies, those skilled in the art are fully enabled to make and use the invention as claimed without undue experimentation. It is further submitted that Applicant reserves the right to pursue the subject matter of the original claims 1-4 and 34-45 in a continuing application.

Accordingly, Applicant respectfully submits that the rejection under 35 U.S.C. §112, first paragraph, is overcome. Withdrawal of the rejection is therefore requested.

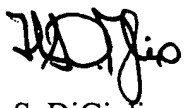
Applicant further respectfully submits that the claims as presently recited are not taught or suggested by any reference of record. Specifically, no reference of record teaches or suggests a genetic construct comprising multiple structural gene sequences placed under the

control of a single promoter, wherein each of said structural gene sequences is identical to a target gene in a cell, and at least one structural gene sequence is placed in the sense orientation under the control of the promoter, and at least one other structural gene sequence is placed in the antisense orientation under the control of the promoter.

Attached hereto is a marked-up version of the changes made to the claims by the instant amendment. The attached is captioned "**Version with markings to show changes made.**"

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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Encl.: Version with Markings to Show Changes Made

Version With Markings To Show Changes Made

IN THE CLAIMS:

Please cancel claims 1-4, 6-35 and 39-45.

Please amend claims 36-38 as follows:

36. (Amended) A [synthetic gene which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell which is transfected with said synthetic gene, wherein said synthetic gene comprises] genetic construct comprising multiple structural gene sequences, wherein each of said structural gene sequences [comprises a nucleotide sequence which] is [substantially] identical to [said] a target gene in a cell [or a derivative of said target gene], and wherein said multiple structural gene sequences are placed operably under the control of a single promoter sequence which is operable in said cell, wherein at least one of said structural gene sequences is placed operably in the sense orientation under the control of said promoter sequence, wherein at least one other of said structural gene sequences is placed operably in the antisense orientation under the control of said promoter sequence, and wherein at least one structural gene sequence that is placed in the sense orientation relative to said promoter and at least one structural gene sequence that is placed in the antisense orientation relative to said promoter are spaced from each other by a nucleic acid stuffer fragment.

37. (Amended) The [synthetic gene] genetic construct of claim 36, wherein at least one structural gene sequence that is in the sense orientation relative to the promoter, said stuffer fragment and at least one structural gene sequence that is in the antisense orientation relative to the promoter form an interrupted palindrome.

38. (Amended) A cell comprising the [synthetic gene] genetic construct of any one of claims [1-3 or 35] 36-37 or 46.

Please add claims 46-47:

46. A genetic construct comprising two structural gene sequences, wherein each of said structural gene sequences is identical to a target gene in a cell, and wherein the two structural gene sequences are placed operably under the control of a single promoter sequence

which is operable in said cell, wherein one of said structural gene sequences is placed o
in the sense orientation under the control of said promoter sequence, wherein the other o
two structural gene sequences is placed operably in the antisense orientation under the c
said promoter sequence, and wherein the two structural sequences are spaced from each other by a nucleic acid stuffer fragment.

47. The genetic construct of any one of claims 36-37 or 46, further comprising at least one of an origin of replication or a selectable marker gene.